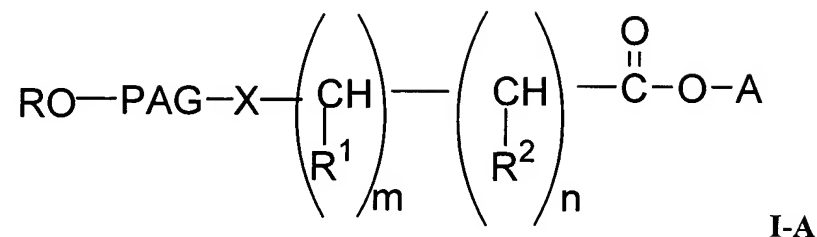


WHAT IS CLAIMED IS:

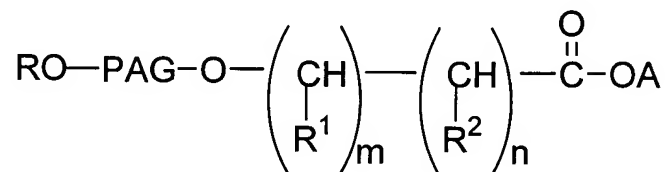
1. A compound of the formula



wherein R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons ; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester

or hydrolyzable esters thereof wherein A is hydrogen.

2. The compound of claim 1 having the formula



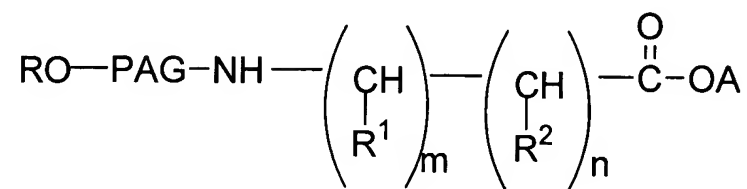
I-A1

wherein A, R, PAG, R<sup>1</sup>, R<sup>2</sup> m and n are as above.

3. The compound of claim 2 wherein A is hydrogen.

4. The compound of claim 3 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
5. The compound of claim 4 wherein R is methyl.
6. The compound of claim 5 wherein n is 0 and m is 4.
7. The compound of claim 5 wherein PEG has a molecular weight of from 10,000 to 40,000.
8. The compound of claim 6 wherein PEG has a molecular weight of from 20,000 to about 35,000.
9. The compound of claim 2 wherein A is an activated leaving group.
10. The compound of claim 9 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
11. The compound of claim 9 wherein R is methyl.
12. The compound of claim 11 wherein n is 0 and m is 4.
13. The compound of claim 12 wherein PEG has a molecular weight of from 10,000 to 40,000.
14. The compound of claim 13 wherein PEG has a molecular weight of from 20,000 to about 35,000.

15. The compound of claim 1 wherein said compound has the formula



I-A2

wherein A, R, PAG, R<sup>1</sup>, R<sup>2</sup>, m and n are as above.

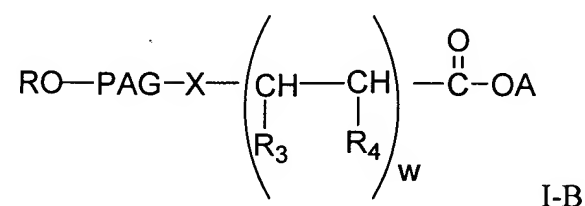
16. The compound of claim 15 wherein A is hydrogen.
17. The compound of claim 16 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
18. The compound of claim 17 wherein R is methyl.
19. The compound of claim 18 wherein n is 0 and m is 4.
20. The compound of claim 19 wherein PEG has a molecular weight of from 10,000 to 40,000.
21. The compound of claim 20 wherein PEG has a molecular weight of from 20,000 to about 35,000.
22. The compound of claim 18 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
23. The compound of claim 22 wherein R is methyl.

24. The compound of claim 23 wherein n is 0 and m is 4.

25. The compound of claim 24 wherein PEG has a molecular weight of from 10,000 to 40,000.

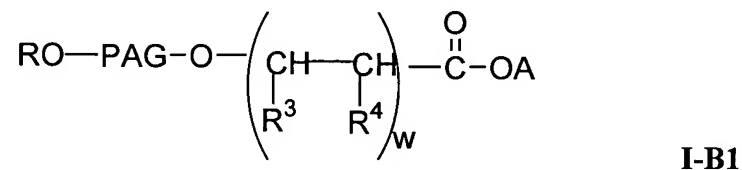
26. The compound of claim 25 wherein PEG has a molecular weight of from 20,000 to about 35,000.

27. The compound of formula



wherein R is hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons ; w is an integer of from 1 to 3; and one of R<sub>3</sub> and R<sub>4</sub> is lower alkyl and the other is hydrogen or lower alkyl; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen forms an ester; or hydrolyzable esters thereof wherein A is hydrogen.

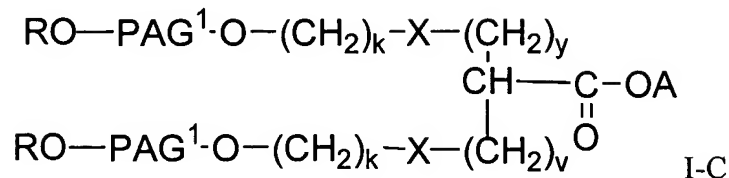
28. The compound of claim 27 wherein said compound is



wherein A, R, PAG, R<sup>3</sup>, R<sup>4</sup>, w and n are as above.

29. The compound of claim 28 wherein A is hydrogen.
30. The compound of claim 29 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
31. The compound of claim 30 wherein R is methyl.
32. The compound of claim 31 wherein w is 1.
33. The compound of claim 32 wherein PEG has a molecular weight of from 10,000 to 40,000.
34. The compound of claim 33 wherein PEG has a molecular weight of from 20,000 to about 35,000.
35. The compound of claim 28 wherein A is an activated leaving group.
36. The compound of claim 35 wherein PAG is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
37. The compound of claim 36 wherein R is methyl.
38. The compound of claim 37 wherein w is 1.
39. The compound of claim 38 wherein PEG has a molecular weight of from 10,000 to 40,000.
40. The compound of claim 39 wherein PEG has a molecular weight of from 20,000 to about 35,000.

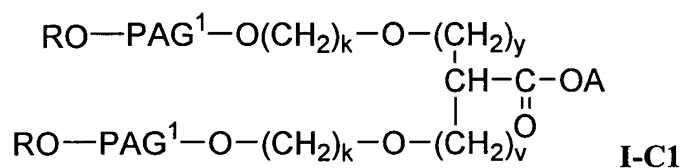
41. The compound of formula



wherein R is hydrogen or lower alkyl, X is -O- or -NH-, A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester, PAG<sup>1</sup> is a divalent residue of a polyalkylene glycol resulting from the removal of both of the terminal hydroxy groups, said residue having a molecular weight of from about 500 to about 25,000 Daltons, y is an integer from 0 to 3 and v is an integer from 1 to 3; and k is an integer from 1 to 2;

or hydrolyzable esters thereof wherein A is hydrogen.

42. The compound of claim 41 wherein said compound has the formula

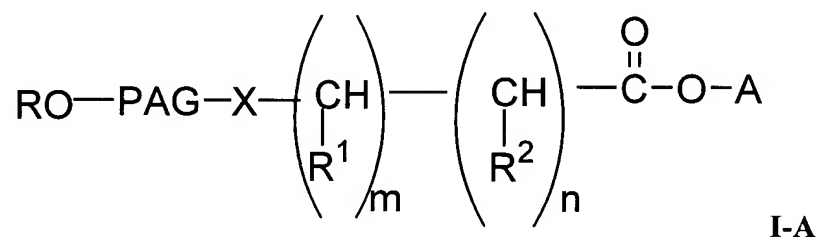


wherein R, PAG<sup>1</sup>, A v, y and k are all as above.

43. The compound of claim 42 wherein A is hydrogen.

44. The compound of claim 43 wherein PAG<sup>1</sup> is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

45. The compound of claim 42 wherein each PAG<sup>1</sup> residue has a molecular weight of 500 to 15,000.
46. The compound of claim 42 wherein A is a leaving group.
47. The compound of claim 46 wherein said leaving group is N-hydroxysuccinimidyl.
48. The compound of claim 47 wherein PAG<sup>1</sup> is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.
49. The compound of claim 48 wherein R is methyl.
50. The compound of claim 49 wherein each PEG residue has a molecular weight of from 500 to 10,000.
51. A process for producing an activated ester of the formula:



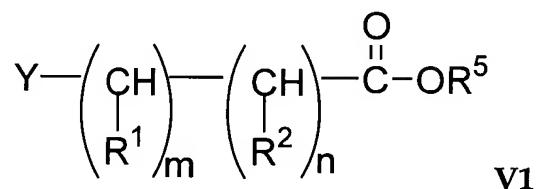
wherein R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a

hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester comprising, condensing a compound of the formula:

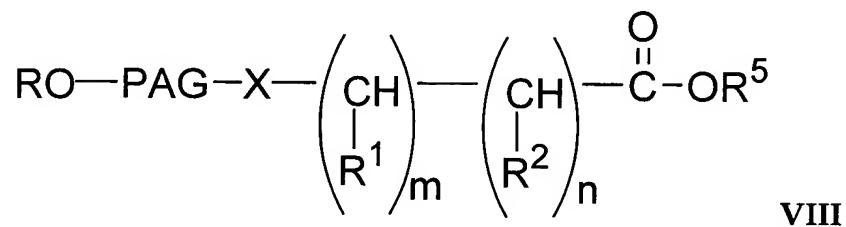


V

wherein R, and PAG are as above, and V is -OH or -NH<sub>2</sub>, with the compound of the formula:

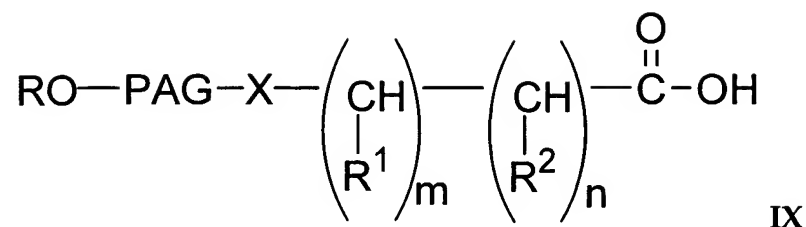


wherein R<sup>5</sup> forms a hydrolyzable ester protecting group and Y is halide and R<sup>1</sup>, R<sup>2</sup>, m, and n, are as above, to produce an ester of the formula



wherein R, PAG, X, R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, m and n are as above, hydrolyzing said ester to form a free acid of the formula:



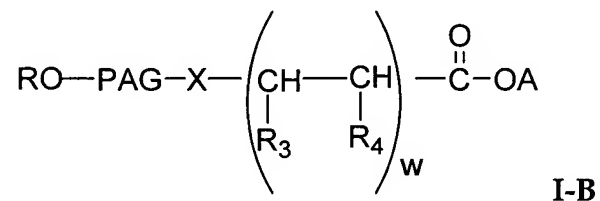


wherein R, PAG, X, R<sup>1</sup>, R<sup>2</sup>, m and n are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

52. The process of claim 51 wherein said leaving group is N-hydroxysuccinimidyl group 58.

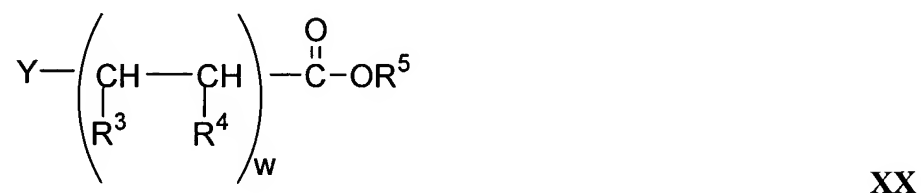
53. A process for producing an activated ester of the formula:



wherein R is hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkyleneglycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; w is an integer of from 1 to 3; and one of R<sub>3</sub> and R<sub>4</sub> is lower alkyl and the other is hydrogen or lower alkyl; and A is a hydrogen or an activated

leaving group which when taken together with its attached oxygen atom forms an ester

comprising, condensing a compound of the formula:



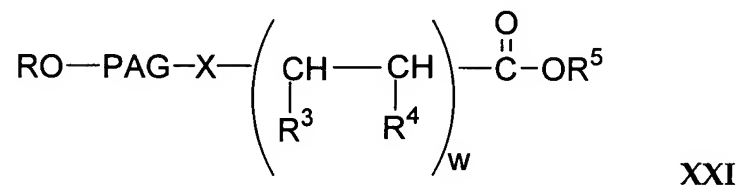
wherein  $w$ ,  $Y$ ,  $R^3$ ,  $R^4$  and  $R^5$  are as above,  $Y$  is halide and  $R^5$  forms a hydrolyzable protecting group

with a compound of the formula:



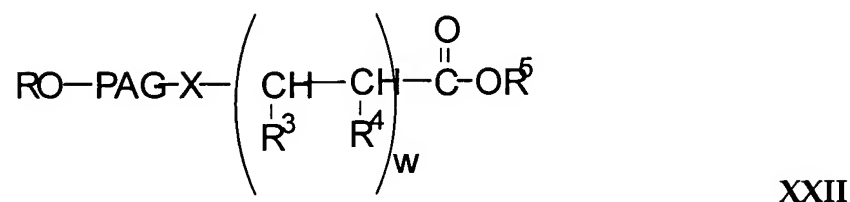
wherein  $R$ , and  $\text{PAG}$  are as above,  $V$  is  $-\text{OH}$  or  $-\text{NH}_2$ ,

to produce an ester of the formula:



wherein  $w$ ,  $R$ ,  $\text{PAG}$ ,  $X$ ,  $R^3$ ,  $R^4$  and  $R^5$  are as above

hydrolyzing said ester to form a free acid of the formula:

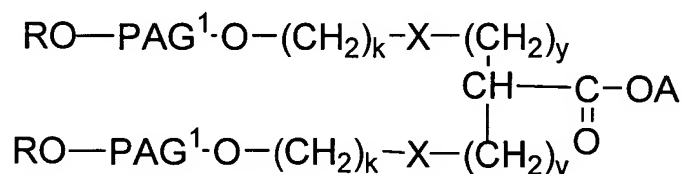


wherein R, PAG, X, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

54. The process of claim 53 wherein said leaving group is a N-hydroxysuccinimidyl group.

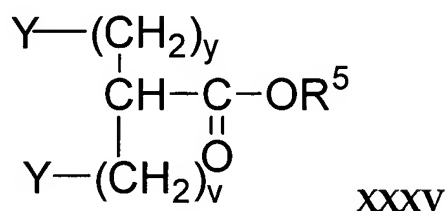
55. A process for producing an activated ester of the formula:



I-C

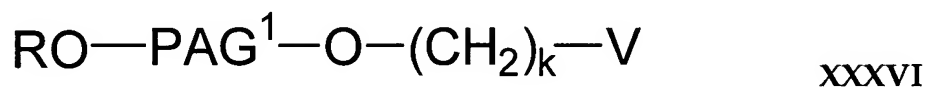
wherein R is hydrogen or lower alkyl, X is -O- or -NH, A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester, PAG<sup>1</sup> is a divalent residue of a polyalkylene glycol resulting from the removal of both of the terminal hydroxy groups, said residue having a molecular weight of from about 500

to about 25,000 Daltons, y is an integer from 0 to 3 and v is an integer from 1 to 3; and k is an integer from 1 to 2, comprising, condensing a compound of the formula:



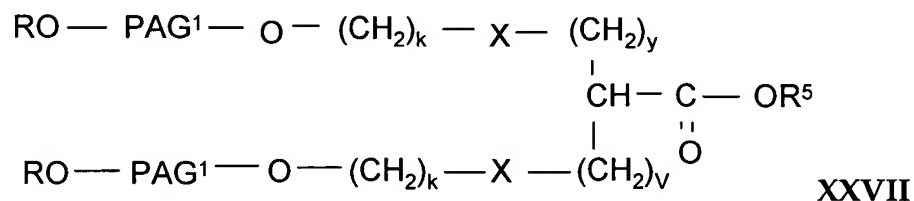
wherein Y is halide, y and v are as above, and R<sup>5</sup> forms a hydrolyzable ester protecting group

with a compound of the formula

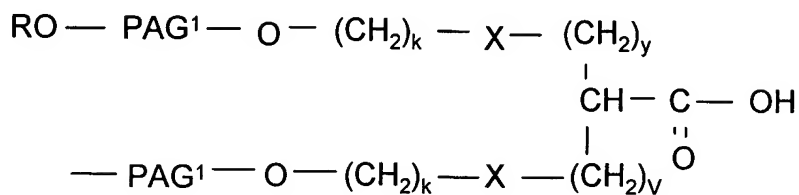


wherein R, PAG<sup>1</sup> and k are as above, V is -OH or -NH<sub>2</sub>,

to produce an ester of the formula:



wherein R, PAG<sup>1</sup>, X, R<sup>5</sup>, k, v and y are as above,



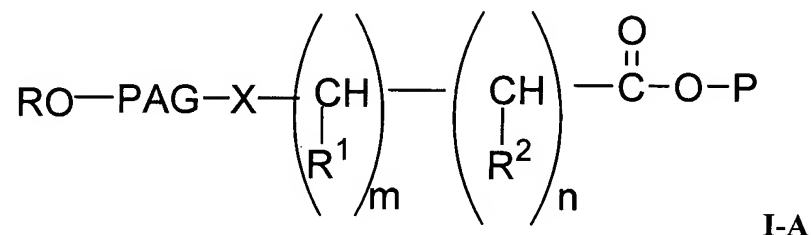
XXVIII

wherein R, PAG<sup>1</sup>, X, k, v and y are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

56. The process of claim 55 wherein said leaving group is N-hydroxysuccinimidyl.

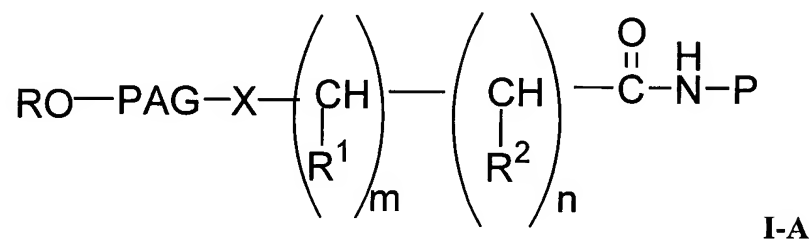
57. A conjugate of the formula



wherein P is a residue of a biopharmaceutical having a terminal hydroxy group wherein the terminal hydroxy group is removed, R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a

molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; and m is an integer of from 4 to 8.

58. The conjugate of claim 57 wherein P is a glycoside.
59. The conjugate of claim 58 wherein P is a residue of AZT.
60. The conjugate of claim 57 wherein X is -O-.
61. The conjugate of claim 60 wherein PAG is a polyethylene glycol residue having a molecular weight of 10,000 to 15,000.
62. A conjugate of the formula



wherein P is a residue of a biopharmaceutical having a terminal hydroxy group wherein the terminal hydroxy group is removed, R, R<sub>1</sub> and R<sub>2</sub> are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; and m is an integer of from 4 to 8.

63. The conjugate of claim 62 wherein P is a residue of a protein or polypeptide.
64. The conjugate of claim 63 wherein X is -O-.
65. The conjugate of claim 64 wherein PAG is a polyethylene glycol residue having a molecular weight of about 10,000 to 15,000.
66. The conjugate of claim 63 wherein P is the polypeptide T-20 having a sequence according to SEQ ID NO: 1.
67. The conjugate of claim 64 wherein R is methyl.